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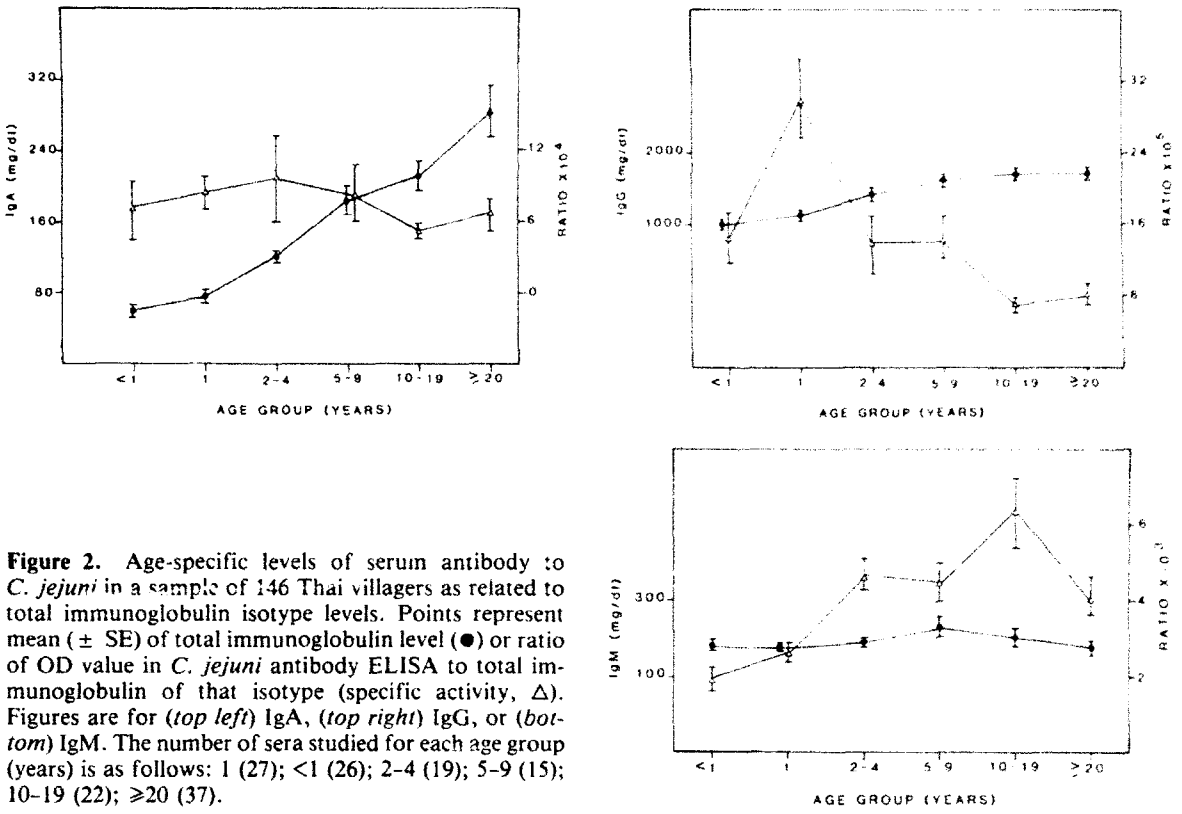

Figure 2. Age-specific levels of serum antibody to *C. jejuni* in a sample of 146 Thai villagers as related to total immunoglobulin isotype levels. Points represent mean (± SE) of total immunoglobulin level (●) or ratio of OD value in *C. jejuni* antibody ELISA to total immunoglobulin of that isotype (specific activity, △). Figures are for (*top left*) IgA, (*top right*) IgG, or (*bottom*) IgM. The number of sera studied for each age group (years) is as follows: 1 (27); <1 (26); 2-4 (19); 5-9 (15); 10-19 (22); ≥20 (37).

It was not until children reached the five- to nine-year age group that the mean serum IgA level (165 mg/dl) reached 80% of the level observed in 20–39-year-old adults (209 mg/dl). This same pattern had been noted for *C. jejuni*-specific IgA (figure 1), and a ratio of the two values (specific activity) was essentially level during life (figure 2, top left). Comparing IgA-specific activities for the various age groupings, we found that none of the distributions were significantly different from one another. The total IgG level in serum changed little after the first few months of life (figure 2, top right). The mean level in children 12–23-months-old (1,195 mg/dl) was 78% of that observed in adults 20–39-year-old (1,535 mg/dl). IgG-specific activity peaked in the 12–23-month age group and then declined to a steady level during older childhood and adulthood. Specific activity in the 12–23-month age group was significantly greater ($P < .001$) than in all the other age groups. The full adult level of total serum IgM was reached between six and 11 months of age and changed little thereafter (figure 2, bottom). IgM-specific activity rose during the first two years of life and peaked in the 10–19-year age group before declining. Specific activity in 10–19-year-olds was significantly greater ($P < .001$) than in children under two years old.

First two years of life. Levels of *C. jejuni*-specific IgG in the cord blood samples (mean, 0.154; median, 0.105; table 1) were nearly identical to the same levels in blood from persons 20–29 years old (mean, 0.150; median, 0.133). Levels of *C. jejuni*-specific IgA and IgM in cord blood were essentially zero, as expected. Levels of antibody to *C. jejuni* of all three immunoglobulin isotypes rose progressively during the first two years of life (table 1). Even accounting for the increase in total immunoglobulin levels of all three isotypes, *C. jejuni*-specific activity rose at faster rates, as evidenced by the ratios calculated (table 1). IgA and IgM specific activity doubled, whereas IgG specific activity went up fivefold during the first two years of life. IgG-specific activity already was significantly higher in children six to 11 months old and remained significantly higher through the first four years of life than in persons >20 years old ($P < .001$). The IgA and IgM specific activities during the first two years of life were not

Table 1. Antibodies to *C. jejuni* during the first two years of life in villagers in rural Thailand.

Antibodies	Cord blood	Age-group (months) 0–5	6–11	12–17	18–23
Antibodies to *C. jejuni**	$n = 30$	$n = 35$	$n = 52$	$n = 17$	$n = 26$
IgA	0.004 ± 0.002	0.029 ± 0.02	0.076 ± 0.02	0.038 ± 0.01	0.096 ± 0.02
	(0)	(0.006)	(0.028)	(0.029)	(0.047)
IgG	0.154 ± 0.02	0.069 ± 0.03	0.313 ± 0.06	0.327 ± 0.07	0.320 ± 0.04
	(0.105)	(0.027)	(0.181)	(0.206)	(0.306)
IgM	0.007 ± 0.001	0.104 ± 0.02	0.438 ± 0.05	0.425 ± 0.066	0.697 ± 0.07
	(0)	(0.054)	(0.362)	(0.435)	(0.658)
Ratio of *C. jejuni* antibodies to total immunoglobulin in that isotype†		$n = 8$	$n = 19$	$n = 12$	$n = 14$
IgA	ND	3.32 ± 0.95	8.22 ± 3.30	5.47 ± 1.02	10.95 ± 2.67
		(2.85)	(3.79)	(4.16)	(6.12)
IgG	ND	6.47 ± 2.60	17.92 ± 3.48	34.09 ± 8.30	28.1 ± 4.64
		(5.87)	(15.49)	(21.6)	(28.8)
IgM	ND	1.20 ± 0.37	2.20 ± 0.32	2.49 ± 0.32	2.72 ± 0.39
		(1.02)	(2.15)	(2.65)	(2.15)

* Data are shown as mean ± SE (median) of OD in ELISA for that immunoglobulin isotype (see Methods for details).
† Data are mean ± SE (median) of ratio of ELISA value to total immunoglobulin isotype (mg/dl) multiplied by 10^4 for IgA, 10^5 for IgG, and 10^3 for IgM.

significantly different from those of persons >20 years old.

Discussion

These Thai villagers show age-related patterns in total immunoglobulin levels similar to those present in all other populations studied [12–17]. However, mean adult levels of IgA, IgG, and IgM are higher than have been observed in adults from developed countries [15–17], but similar to those in Gambian [13] and other African and Thai adults [12]. This phenomenon may represent an increased production of immunoglobulins, either on an environmental or a genetic basis [9]. However, similar high levels in several populations in developing countries lessens the likelihood of genetic factors, but correlates with high levels of exposure to a variety of pathogenic microorganisms.

Levels of antibody to *C. jejuni* in rural Bangladeshi children previously have been studied [7]; we now report results from a second locale of the developing world. In this investigation we studied a greater number of samples from persons of all ages who previously had been studied for antibodies to other enteric pathogens [10], and levels of specific antibodies to *C. jejuni* were compared with levels of total immunoglobulin isotypes. Nearly every villager acquired antibody to rotavirus and hepatitis A in early childhood, and antibodies persisted for life [10]. Antibodies to Norwalk virus were acquired during the preschool years by ~60% of the population and were retained for life. In contrast, the seroprevalence of antibody to the heat-labile enterotoxin of *Escherichia coli* was highest among children between one and four years old and then declined. The peak age for prevalence of this neutralizing antibody, chiefly IgG, is similar to the age in the same population at which we observed peak levels of IgG antibody to *C. jejuni*.

The patterns that we observed in the ELISAs specific for *C. jejuni* immunoglobulin isotype are very similar to those previously observed in Bangladeshi children [7]. IgG levels peaked earlier in the Thai children, but specific IgA levels rose through childhood in both groups. Studies in Thai adults showed that specific serum IgA increases progressively and may represent a marker for total lifetime exposure to *Campylobacter* organisms, and thus immunity. Specific serum levels of IgA correlate with resistance of mice to infection with *Salmonella typhimurium* after oral immunization with various salmonellae [18]. The IgM plateau found in older Bangladeshi children was found in Thai children, but levels declined in older persons. This study confirms that

in endemic areas levels of serum IgA antibodies to *C. jejuni* rise during life, whereas IgG peaks early in life and then falls. Whether the rising serum levels of IgA reflect rising gut immunity should be tested by prospectively comparing stool and serum antibodies to *C. jejuni* in infected and control children in an endemic area. Whether this phenomenon is a model for other enteric infections in which host populations are repeatedly exposed to a particular pathogen is a hypothesis that also should be tested.

That specific activity of IgA to *C. jejuni* was level despite the progressive age-related rise in IgA to *C. jejuni* suggests that exposure to *C. jejuni* antigens is continual and occurs at equal rates for the different age-groups with respect to other stimuli of serum IgA production. The age-associated prevalence of *C. jejuni* infection, as determined by a single culture, falls with age in Bangladesh [2, 3], but because median duration of excretion after infection also falls with age in that population [6], actual exposure rates may be more nearly equal in different age groups. Support for this conjecture comes from the recent observation [19] among Japanese children with *C. jejuni* infection that duration of convalescent excretion was briefer in those with serum antibody to specific cellular antigens than in those without. Conversely, hypogammaglobulinemic children have prolonged convalescent excretion of these organisms [20].

Antibodies to *C. jejuni* rose at higher rates during the first two years of life than did the total immunoglobulins of all three isotypes (table 1), a result correlating with the intense early exposure to *C. jejuni* noted in culture surveys in other developing areas [1–6] and in Soongnern [21]. Because determining the age-related prevalence of antibody to gastrointestinal pathogens provides important information for assessing the potential value of immunization for the control of enteric disease in different populations [22], these data suggest that the greatest potential impact of a vaccination campaign against *C. jejuni* would be early in life, before numerous natural infections had occurred.

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